REMARKS

This amendment is filed in response to a telephonic interview with the Examiner, to expedite allowance of the application following the reopening of prosecution. The Office reopened prosecution after registered attorney Valerie E. Looper filed a protest on behalf of an unidentified protester, even though the protest was untimely under 37 CFR 1.291. In a brief telephonic interview on February 23, and in a subsequent interview summary, the Examiner suggested that Applicants further amend independent claims in view of the protest, if the Applicants wished to preempt a reopening of prosecution in view of the Vaeck reference.[1]

To expedite re-allowance of the case, the Applicants have amended claims 51 and 67, as explained below in Sections I. and II.

I. CLAIM 51 IS PATENTABLE OVER THE ART RELIED UPON IN THE PROTEST AND THE PRIOR ART AS A WHOLE.

The protester alleged that claim 51 was anticipated by Vaeck et al. as supported by Höfte et al. and Beck et al.[2] Each of these publications was previously made of record and considered by the Office during prosecution: Vaeck et al, (1987) (Document C188 in IDS dated 12/15/06) ("Vaeck"); Hofte (1986) (Document C80 in IDS dated 12/15/06); and Beck et al (1982) (Document C16 in IDS dated 12/15/06).

Vaeck purports to have attached a kanamycin resistance gene (*neo*) to the 3' terminus of a truncated a *bt2* toxin gene from *Bacillus*. For purposes of this discussion, Vaeck's resultant sequence will be called Vaeck's "truncation-fusion" gene.

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[1] The fourth sentence of the interview summary states, "Vaeck deleted insecticidal protein coding sequence and replaced it with sequence encoding another protein." (It is not clear if this sentence is intended as an observation of the Examiner or a memorialization of some portion of the interview.) The intended meaning of "insecticidal protein coding sequence" in this sentence is unclear. Vaeck describes constructs that are lacking the C-terminal portion of a wild type *bt2* coding sequence. The protein encoded by the wildtype gene is an insecticidal protein; the portions that are absent in Vaeck's constructs are not portions that confer insecticidal activity. Also, the Applicants reserve the right to dispute any allegation that Vaeck "deleted." (See Footnotes 4 below.)

[2] The primary reference relied upon by the protester was Vaeck. The protester cited Höfte et al. stating it contained a published sequence for the endotoxin in Vaeck et al. and Beck et al. stating it contained a published sequence for the neo gene used in the Vaeck et al. reference. (See protest at pages 3-4.)

The Applicants dispute any allegation, in the protest or otherwise, that Vaeck (or any other cited art) anticipates or renders obvious (alone or in combination with other art) any claim as previously presented. In fact, the protester did not even attempt to apply the cited art to any claim except claim 51, and did not attempt any obviousness analysis.

Notwithstanding the foregoing, the Applicants have amended claim 51 herein in two different ways to expedite allowance. (The second version of claim 51 is presented as new claim 164.[3])

Step (b) of amended claim 51 now reads, "(b) reducing the number of said ATTTA sequences and the number of said polyadenylation signal sequences in said portion of the coding sequence by substituting sense codons for codons in said portion, wherein said substituted sense codons maintain the original encoded amino acids." Basis for such amendments includes, for example, page 59 of the specification, which describes making alterations while maintaining the original encoded amino acid sequence. If, for the sake of argument, Vaeck's *neo* codons are treated as substituted codons,[4] Vaeck's method still fails to meet the limitations of amended claim 51 pertaining to said substituted sense codons maintaining the original encoded amino acids.

New claim 164 specifies making changes to *an insecticidal portion* of a *B.t.* sequence:

> (a) starting with an insecticidal portion of a coding sequence ...;
>
> (b) reducing the number of said ATTTA sequences and the number of said polyadenylation signal sequences in said insecticidal portion of the coding sequence by substituting sense codons for codons in said portion; and
>
> (c) making a structural gene that comprises said insecticidal portion with the substitute codons and the reduced number of ATTTA and polyadenylation signal sequences....

Vaeck purportedly attached an insecticidal portion of a *bt2* coding sequence (the amino terminal portion) to a *neo* coding sequence to make a sequence coding for a fusion protein. However one characterizes Vaeck's method, Vaeck did NOT reduce the number of

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[3] Should claim 164 be allowed, the Applicants request the opportunity to make existing dependent claims dependent from claim 164 as well.

[4] The Applicants reserve the right to contest any assertion that Vaeck substituted codons in the sequence with which Vaeck started.

ATTTA or polyadenylation signal sequences in the insecticidal portion of Vaeck's *B.t.* sequence. Thus, the limitations of new claim 164 are not met, and are not suggested.

The protester has argued that Vaeck "substituted" codons for the C-terminal portion of (a full length) *B.t.* sequence, thereby reducing the total number of ATTTA or polyadenylation sequences relative to such original (full length) *B.t.* sequence. However, such "substitutions" were made relative to the C-terminal portion of a *B.t.* sequence – a portion that Vaeck did not use, and that did not confer the insecticidal activity. Because Vaeck's process did not reduce the number of ATTTA sequences and the number of polyadenylation signal sequences in an insecticidal portion of a coding sequence, Vaeck neither discloses nor suggests the method of new claim 164.

New claim 164 is similar to previous claim 51 except for the additional language specifying alterations to an "insecticidal" portion of the gene. This language finds support throughout the specification, including, e.g., Examples 1 and 2. Example 1 describes a variety of structural gene embodiments generated through site-directed mutagenesis. In some embodiments, approximately the amino-terminal one-third of a wildtype B.t.k. HD-1 gene (residues 29-607) was altered to reduce the number of problem (ATTTA or Table II polyadenylation signal) sequences. Site-directed mutagenesis reduced the number of polyadenylation sequences from 18 to 7 and the number of ATTTA sequences from 13 to 7, achieving modified sequences that exhibited improved expression in plants. In still other variations, within the amino-terminal one third of the gene, the inventors made alterations to approximately the first third (bases 1-590) or the second two thirds (bases 590-1845). Both constructs were expressed and resulted in insect toxicity. (See page 45, lines 1-26) Example 2 describes an experiment in which a synthetic insecticidal fragment (amino acids 1-615) of Btk HD-1 was made that was devoid of ATTTA sequences and substantially devoid of Table II polyadenylation signal sequences (in this instance, only one). (See, e.g., page 50, line 25, through page 51, line 2.)

II. CLAIM 67 IS PATENTABLE OVER THE ART RELIED UPON IN THE PROTEST.

First, it should be noted that the protester has alleged that Vaeck started "with a portion of a coding sequence." (Protest at p. 5.) Claim 67 specifies starting with an amino

acid sequence, and the protester has not articulated how Vaeck applies to any claim that involves starting with an amino acid sequence.

In the interview, the Examiner expressed concern that claim 67 would read on Vaeck insofar as Vaeck's truncated *B.t.* coding sequence includes a portion of Vaeck's wild type *B.t.* coding sequence, and the included portion contained fewer of the ATTTA and fewer of the polyadenylation signal sequences than the original *full length* wild type sequence. This concern is rendered moot by amendment.

Step (b) of amended claim 67 requires making a structural gene that has a reduction in the number of the ATTTA and polyadenylation sequences (relative to wild type) in the portion that is included in the structural gene, not merely a reduction due to truncation of the wild type gene. Vaeck did not change the number of ATTTA or the number of polyadenylation signal sequences in the insecticidal portion of Vaeck's *B.t.* sequence that Vaeck used to make Vaeck's truncation-fusion. To clarify that claim 67 does not read on Vaeck's truncation, the final step of claim 67 has been amended to specify, "(b) making a structural gene that encodes an insecticidal protein and that comprises a coding sequence that encodes the amino acid sequence of the portion and that contains fewer ATTTA sequences and fewer of said polyadenylation signal sequences than the wild-type *B.t.* coding sequence from which said portion was derived." The term "said portion" refers back to starting portion in step (a). With this clarifying amendment, the method of claim 67 is neither disclosed nor suggested by Vaeck.

III. CLAIM 47 IS PATENTABLE OVER THE ART OF RECORD.

The Examiner identified claim 47 in the interview and the interview summary. Independent claim 47 specifies (in part) "starting with a coding sequence ... that encodes an insectidical protein...;" and further specifies "making a structural gene that ... encodes the insecticidal protein." If Vaeck is construed to have started with a full length *bt2* coding sequence, then Vaeck did not meet these limitations of claim 47: Vaeck did not make a structural gene that encodes the (full length) protein, because Vaeck's truncation-fusion lacks a major portion of the *bt2* coding sequence.

If, on the other hand, Vaeck is construed to have started with a truncated (N-terminal) *bt2* coding sequence, or started with a coding sequence for the truncation-fusion construct, then Vaeck fails to meet other limitations of claim 47: limitations in steps (b) and

(c) relating to reducing problem sequences. Step (b) of claim 47 specifies reducing the number of polyadenylation signal sequences in the coding sequence by substituting sense codons, and step (c) specifies making a structural gene that includes the codons substituted in step (b). If Vaeck's starting sequence encodes the N-terminal truncation of *bt2*, or the whole truncation-fusion construct, then Vaeck did not substitute codons to reduce polyadenylation signal sequences as specified in claim 47.

In summary, there is no interpretation of Vaeck that can be said to disclose or suggest the method of claim 47. Thus, claim 47 is patentable over Vaeck.

IV. THE REMAINING CLAIMS ARE PATENTABLE OVER THE ART OF RECORD.

The protester alleges in the protest that the cited art also *anticipates* claim 59, 60, 67, 119, 120, 121, 124, 125, 127; and *renders obvious* claims 47, 49, 55, 113, 114, 115, 122, 123, 148, 149, 155, 156, and 159-162. The protester fails to even attempt to apply the cited reference(s) to any of the claims except claim 51, so the protest cannot fairly be said to raise any issues with respect to these other claims. The protest alleges that claim 51 is "representative." In fact, each of the cited claims has different limitations, so claim 51 cannot be deemed "representative" of any other claim. The only other claims discussed during the interview are treated above.

V. CONCLUSION.

The protest as filed has no merit, and does not even attempt to make a *prima facie* case of unpatentabilty against any claim except claim 51. Claims 51 and 67 have been further amended herein, and differences between these claims and the prior art are set forth in the remarks above. All of the claims define methods that are neither disclosed nor suggested by Vaeck or other prior art of record, and do not require further amendment. Accordingly, favorable reconsideration and allowance is respectfully requested.

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Respectfully submitted,

By /David A. Gass #38,153/
David A. Gass
Registration No.: 38,153
MARSHALL, GERSTEIN & BORUN LLP
233 S. Wacker Drive, Suite 6300
Chicago, Illinois 60606-6357
(312) 474-6300
Attorney for Applicants